

REMARKS/ARGUMENTS

Reconsideration of this Application and entry of this Amendment are respectfully requested.

By the amendments, Applicants do not acquiesce to the propriety of any of the Office's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

In the Claims

Claims 5, 7, 10-13, 15-16 are pending in this application. Claims 1-4, 6, 8-9, and 14 have been previously canceled.

Claim 5 has been amended to recite the step of inhibiting mycobacterial glutamine synthetase to a greater degree than mammalian glutamine synthetase, and wherein gamma-glutamylcysteine synthetase or glutathione synthesis are not substantially inhibited, support for which is found in, for example, paragraph [0013] of the published specification.

Claims 17-22 are newly added. Support for claims 17-22 can be found in, for example, the previously pending claims as well as paragraph [0013] of the published specification.

No new matter has been introduced as a result of the claim amendments.

Withdrawn Rejections

The Applicants would like to thank the Office for withdrawing the rejections as listed on Pages 2 and 3 of the Office Action mailed September 12, 2008. For the sake of brevity, those withdrawals will not be listed here.

Rejections under 35 U.S.C. §102

Claims 5, 7, 12, 13, 15 and 16 have been rejected under 35 U.S.C. §102(b) as being anticipated by Stamler et al. (U.S. Pat. 6,057,367, hereinafter "Stamler"). The

Office asserts that Stamler discloses a method of killing or reducing the growth of pathogenic microbes in mammals such as humans by selective manipulation of nitrosative stress. The Office further suggests that one skilled in the art would envisage the compounds taught in Stamler as including the specific S-methyl compound, which is a methionine sulfoximine according to the instant claims. The Applicants respectfully disagree.

As the Office is aware, to anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 224 USPQ 409, 411 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements "arranged or combined in the same way as in the claim." *Net MoneyIN, Inc. v. Verisign, Inc.*, 2007-1565, (Fed. Cir. 2008). Finally, the law requires identity between the claimed invention and the prior art disclosure. *Kalman v. Kimberly-Clark Corp.*, 218 USPQ2d 781, 789 (Fed. Cir. 1983, cert denied, 465 U.S. 1026 (1984)).

The Applicants assert that claims 5, 7, 12, 13, 15 and 16 recite a method of treating, palliating or inhibiting mycobacterial infections in a mammal by inhibiting mycobacterial glutamine synthetase without causing substantial toxic side effects in the mammal and furthermore include the step of inhibiting mycobacterial glutamine synthetase to a greater degree than mammalian glutamine synthetase. Stamler does not disclose a method of inhibiting mycobacterial glutamine synthetase but rather teaches a method of "manipulating nitrosative stress to kill or reduce the growth of pathogenic microbes or pathogenic helminthes or pathogenically proliferating mammalian cells" (Stamler, column 1, lines 56-59, emphasis added). Stamler further teaches that nitrosative stress is "an impetus for NO or NO₂ group attachment to proteins, nucleic acids or other biological molecules" (Stamler, column 2, lines 1-3). One skilled in the art understands that manipulating NO and NO₂ attachment to biological molecules and inhibiting a protein such as glutamine synthetase are not the same.

Furthermore, amended claim 5 requires that the method not result in the inhibition of gamma-glutamylcysteine synthetase, an enzyme specifically inhibited by the compounds of Stamler (see Stamler, column 14 lines 65 to column 15 line 12).

As such, Stamler does not disclose each and every limitation of the present claims. Stamler does not teach a method of inhibiting mycobacterial glutamine synthetase, but rather, teaches a method of manipulating nitrosative stress. Furthermore, Stamler teaches inhibition of gamma-glutamylcysteine synthetase. The present claims include the limitation wherein gamma-glutamylcysteine synthetase or glutathione synthesis are not substantially inhibited. Stamler does not teach or suggest this limitation. As such, the Applicants request the Office withdraw the 35 U.S.C. §102(b) rejection of claims 5, 7, 12, 13, 15 and 16.

Rejections under 35 U.S.C. §103

Claim 11 is rejected under 35 U.S.C. §103(a) as being obvious over Stamler in view of the Merck Manual of Diagnosis and Therapy, Seventeenth Edition. (hereinafter "Merck"). The Office Asserts that Stamler discloses a method of killing or reducing the growth of pathogenic microbes in mammals such as humans by selective manipulation of nitrosative stress. The Office admits that Stamler does not disclose a method further comprising administering isoniazid. The Office attempts to combine Stamler with Merck, which discloses that isoniazid is a commonly used drug for the treatment of tuberculosis and is used in combination with other therapeutic agents. The Office, therefore, asserts that claim 11 would be *prima facie* obvious over Stamler in view of Merck. The Applicants respectfully disagree.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Indeed, as the Board of Patent Appeal and Interferences has recently confirmed, a proper obviousness determination requires that the Office make "a searching comparison of the claimed invention - *including all its limitations* - with the teaching of the prior art." See *In re Wada and Murphy*, Appeal 2007-3733, citing *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis in original). Further, the

necessary presence of all claim features is axiomatic, since the Supreme Court has long held that obviousness is a question of law based on underlying factual inquiries, including ... ascertaining the differences between *the claimed invention* and the prior art. *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966).

The Applicants assert that claim 11 recites a method of treating, palliating or inhibiting mycobacterial infections in a mammal by inhibiting mycobacterial glutamine synthetase without causing substantial toxic side effects in the mammal in combination with the administration of isoniazid. As discussed *supra*, Stamler does not teach or suggest of a method of inhibiting mycobacterial glutamine synthetase but rather teaches a method of "manipulating nitrosative stress to kill or reduce the growth of pathogenic microbes or pathogenic helminthes or pathogenically proliferating mammalian cells" (Stamler, column 1, lines 56-59, emphasis added). Stamler further teaches that nitrosative stress is "an impetus for NO or NO₂ group attachment to proteins, nucleic acids or other biological molecules" (Stamler, column 2, lines 1-3). One skilled in the art understands that manipulating NO and NO₂ attachment to biological molecules and inhibiting a protein such as glutamine synthetase are not the same.

Furthermore, Stamler teaches inhibition of gamma-glutamylcysteine synthetase. The present claims include the limitation wherein gamma-glutamylcysteine synthetase or glutathione synthesis are not substantially inhibited. Stamler does not teach or suggest this limitation.

Therefore Merck, which teaches the therapeutic uses of isoniazid, does not remedy the deficiencies of Stamler. Therefore, the combination of Stamler and Merck does not teach or reasonably suggest each and every limitation of claim 11. As such, the Applicants assert the Office has not established a *prima facie* case of obviousness against claim 11 and respectfully request withdrawal of the 35 U.S.C. §103(a) rejection of claim 11.

Double Patenting

Claims 5, 7, 10-13, and 15-16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Pat. No. 6,057,367 (Stamler)

For the reasons discussed below, Applicants traverse the obviousness-type double patent rejection over claims 1-6 of Stamler. The policy behind the judicially-created doctrine of obviousness-type double patenting is "to prevent the unjustified or improper timewise extension of the 'right to exclude' granted by a patent." However, the Applicants respectfully submit that allowance of the Applicants' pending claims 5, 7, 10-13, and 15-16 would clearly not lead to an improper timewise extension of the claims in Stamler.

Claims 1-6 of Stamler cover a method of using an "antiproliferative effective amount of one or more manipulators of nitrosative stress... whereby nitrosative stress selectively kills or reduces the growth of said microbes or of said helminths or of said mammalian cells" (Stamler, claim 1) . Claims 5, 7, 10-13, and 15-16 of the instant application recite methods of treating, palliating or inhibiting mycobacterial infections in a mammal by inhibiting mycobacterial glutamine synthetase without causing substantial toxic side effects in said mammal and require the inhibition of mycobacterial glutamine synthetase to a greater degree than mammalian glutamine synthetase while not inhibiting gamma-glutamylcysteine synthetase or glutathione synthesis. The Applicants respectfully submit that the two methods are patentably distinct, and the present claims would not be obvious in light of the claims in Stamler.

Thus, the methods recited in claims 1-6 of Stamler do not read on the methods recited in claims 5, 7, 10-13, and 15-16 of the instant application. Additionally, there is nothing in the art that teaches or suggests that the methods covered by the Applicants' claims are equivalent to the methods covered by the claims of Stamler, which would allow the Applicants to make a claim that someone using the methods covered by Stamler would be infringing the Applicants' claims. Moreover, the Applicants' claims are not just obvious variations of claims 1-6 of Stamler that would extend its patent term.

Therefore, Applicants respectfully assert that claims 5, 7, 10-13, and 15-16 of the instant application are not obvious over claims 1-6 of Stamler, and request withdrawal of the obviousness-type double patenting rejection on this basis.

Conclusion

In light of the claim amendments and the arguments presented *supra*, Applicants respectfully assert that the pending claims are in condition for allowance. Further, Applicants assert that new claims 17-23 are also in condition for allowance. As such, the Applicants request the Office issue a timely Notice of Allowance in this case.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 50-3207.

Respectfully submitted,

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